BENEFITS OF VOLUME LOADING AFTER PULMONARY EMBOLISM IN DOGS WITH OPEN PERICARDIA

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Volume loading (VL) is frequently recommended for circulatory collapse due to pulmonary embolism (PE). We previously documented that VL after experimental PE caused increased pericardial (PER) pressure (P), leftward septal shift (LSS) and decreased LV volume and stroke work (SW). To clarify the contribution of the PER to the hemodynamic deterioration, we studied 6 open-chest dogs with open PER. PLV, PRV, septum-to-LV free wall (DSLV) and LV anteroposterior (DAP) diameters (sonomicrometry) were measured. Repeated PE (RPE) was produced with autologous clot. VL was performed before PE (BPE), after 1PE (A1PE), and after RPE (ARPE). LV area (ALV=DAPxDSLV) was used as an index of LV volume. LV SW was calculated as the PLV-ALV loop area.

	ALV (mm^2x10)		SW (mm Hgxmm^2)	
	C	VL	C	VL
BPE	325±70	376±60*	252±122	497±182*
A1PE	337±68	357±67*	289±145	320±206*
ARPE	331±60	350±58*	261±158	425±170*

*p<.05 vs. C (ANOVA)

Thus, in the absence of pericardial contraint, repeated embolism did not decrease either ALV or LV SW. Moreover, in contrast to what has been shown to occur in intact animals, volume loading after embolism increased (rather than decreased) ALV and LV SW. We therefore conclude that pericardial constraint is a major mechanism of the adverse effects of experimental pulmonary embolism and subsequent volume loading.

NEURAL MODULATION OF OPTIMAL VENTRICULO-ARTERIAL COUPLING IN CONSCIOUS DOGS

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Stroke work maximization, a theoretically proposed criterion for optimal ventriculo-arterial coupling, does not always hold true for human cardiovascular system. To resolve this contradiction, we used 8 conscious dogs chronically instrumented with micromanometer and conductance catheter and examined reflex autonomic control of ventriculo-arterial coupling. All dogs were studied while autonomically intact, and 6 were studied after autonomic blockade. The LV contractile properties were quantified by the slope of end-systolic pressure-volume relation (Ees). The arterial system properties were expressed by the slope of end-systolic pressure-stroke volume relation (Ea). Within the coupling framework, stroke work can be maximized when Ees and Ea are equalized (Ea/Ees=1). Under autonomically intact conditions, Ea/Ees was 1.4±0.2 (mean±SD) which was considerably larger than the value at optimal stroke work. During nitroprusside infusion, Ees rose by 65% ($p<0.05$) while Ea remained unchanged, hereby Ea/Ees fell to 0.8±0.3 ($p<0.01$). These changes were associated with arterial pressure maintained normal. After autonomic blockade, Ea/Ees became 0.9±0.1. During nitroprusside infusion, Ees decreased by 16% ($p<0.05$) together with a 14% ($p<0.05$) reduction in Ea resulting in the same Ea/Ees (0.9±0.1), hereby the ventricle generated optimal stroke work. However, arterial pressure fell substantially to unphysiological level. Thus, the reflex control of arterial pressure predominates over the maximization of stroke work in ventriculo-arterial coupling in conscious dogs.

RELAXANT EFFECTS OF ISOPROTERENOL IN ISOLATED MYOCARDIUM: INFLUENCE OF THE LOAD LEVEL

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Isoproterenol (iso) is known to increase the myocardial lengthening velocity and the peak rate of force decline. We tested the hypothesis that the relaxant effects of iso depended upon the level of load faced by the muscle. Responses to 0.5mM calcium and cumulative doses of iso (10^{-10}, 10^{-9}, 10^{-8}, 10^{-7}, 10^{-6} M) were studied in 20 left ventricular papillary muscles of Wistar rats, stimulated 12/mn at 29°C. We measured maximum unloaded shortening velocity (Vmax), positive (+dF) and negative (-dF) peak force derivative of the full isometric twitch, and peak lengthening velocity of the isotonic twitch with preload only (V_L). As compared to their control values before iso, both Vmax and +dF significantly increased under iso 10^{-10}M ($p<0.01$ and $p<0.02$ respectively). Similarly, in the full isometric twitch, -dF increased under iso 10^{-10}M (111 +/-13 vs 96 +/- 12mN/sec, $p<0.01$). Conversely, under low loading conditions, i.e., in the twitch with preload only, V_L significantly increased under iso 10^{-8}M only (1.66 +/- 0.14 vs 1.44 +/- 0.17 Lmax/sec, $p<0.02$). Thus, the positive inotropic effect of iso seemed independent of the level of load whereas there was a one hundredfold dose difference in the relaxant effect of iso when low and heavy loading conditions were compared.

This suggests a load-revealed dose dependence of the various biochemical processes involved in the effects of the drug during diastole, but not during systole.

THE RELATIONSHIP BETWEEN CHANGES IN EJECTION FRACTION AND CHANGES IN VENTRICULAR ARRHYTHMIA FREQUENCY: EFFECT OF PHARMACOLOGIC INTERVENTION.

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Left ventricular function (EF) and arrhythmia frequency (VPC) may be influenced by antiarrhythmic therapy (AA). In addition, arrhythmia suppression and possible aggravation with AA may relate directly to LV function. Therefore, the relationship between the changes in EF and VPC frequency was tested in 108 patients using ambulatory ECGs before and after AA therapy. The intra-individual changes in EF and VPC frequency were plotted for the entire group and the relationship was tested using multiple linear regression analyses. There was no relationship between individual % changes in EF and arrhythmia suppression or aggravation for the entire group. AA reduced VPC/hr in Group I (EF≥40%, 78 pts) from 421 ±513 to 128 ±204 ($p<0.0001$) and in Group II (EF<40%, 30 pts) from 398 ±450 to 77 ±100 ($p<0.0003$). Forty two of 78 patients (54%) in Group I and 19 of 30 patients (63%) in Group II had ≥75% of VPCs (p=NS for groups). Thus, changes in EF bear no relationship to arrhythmic suppression or aggravation even in the subgroup with left ventricular dysfunction. AA suppresses equally, VPC frequency in the presence of normal and abnormal LV function.